

### **REMARKS/ARGUMENTS**

Claims 1-5, 7, 15, 17-23, 27, 31, 32, 35-37 and 39 are pending in the application. Claims 1-5, 7, 35-37 and 39 are withdrawn from consideration. Claims 15, 17-23, 27, 31 and 32 are rejected by the Examiner. Claim 21 has been canceled, without prejudice. Claim 15 has been amended to clarify that tissue samples are dissociated via enzyme agents in the tissue dissociation chamber, to recite that the tissue dissociation chamber is in fluid communication with the tissue disruption channel. In addition, claim 15 is further amended to render more explicitly that the tissue disruption channel comprises at least one region of constriction, such that within the region of constriction, the tissue disruption channel has a smaller cross-sectional area as compared to the average cross-sectional area of the tissue disruption channel. Support for these amendments are found throughout the original application as filed, *see, e.g.*, at Figure 12, and page 33, line 14 to page 34, line 14 of the application as originally filed.

Clarifying amendments have also been made to claims 17-20, 22, 23 and 27. In particular, support in the original disclosure for the amendment to claim 18 may be found, *e.g.*, at page 8, lines 18-25 and page 9, lines 10-12 of the application as originally filed. Support for the amendment to claim 19 is found, *e.g.*, at page 22, line 1 to page 23, line 5 of the application as originally filed. Other than minor editorial amendments, no other amendments have been made to the remaining claims. No new matter is added by the present amendments, nor do the amendments entail additional search of the relevant art.

#### **Rejections under 35 USC § 112**

The Examiner has rejected claims 15, 17-23, 27, 31 and 32 as being indefinite and failing to particularly point out and distinctly claim the subject matter that the applicant regards as the invention. Applicants will address each of the Examiner's specific rejections in turn.

##### **a) Claim 15 – page 3, second paragraph**

The Examiner states at page 3 of the Office Action that the word “enzymolytic” is not a term of art. The Applicants disagree with the Examiner. In particular, Applicants believe that reference to “an enzymolytic tissue dissociation chamber” in claim 15 would be clear to one of ordinary skill in the art. Nevertheless, in an effort to facilitate prosecution of this invention, Applicants have amended the relevant applicable claims so that this specific term is not recited while still clearly retaining the intended meaning of the claims.

Further, Applicants have also amended claim 15 to clarify that the dissociation of the tissue samples take place via the administration of enzymes to the samples within the “tissue disassociation

chamber” of the present invention. Applicants observe that “tissue dissociation” is described at, *e.g.*, page 12, lines 9-16 of the application as originally filed. It is clear from this description that the tissue dissociation takes place in a chamber as a result of application of at least one enzyme and that the “chamber” itself is not dissociated. Applicants trust that these minor adjustments to the claims have clarified the intended meaning and scope of the claim terms as recited and thus obviated the grounds for rejection.

b) Claim 15 – page 4, first full paragraph

The Examiner, at the first full paragraph of page 4 of the Office Action, has stated that claim 15 is incomplete in that it omits essential structural cooperative relationships of elements. Without conceding that the Examiner is correct, but rather for purposes of expediting the prosecution of the present application, the Applicants have amended claim 15 to recite that the tissue dissociation chamber is in fluid communication with the tissue disruption channel. A person of ordinary skill in the art, referring to (for example) page 33, lines 26-28 of the application as originally filed, would readily understand the device to contain a fluid. In view of the above, the Applicants submit that the amendment to claim 15 clarifies the claim in such manner as to allay the Examiner’s concerns and Applicants therefore ask that the Examiner reconsider and withdraw the rejection to claim 15.

c) Claims 17, 18 and 19 – page 4, first full paragraph; page 5, paragraphs 1-4

The Examiner is of the opinion that claims 17, 18 and 19 do not indicate how the chambers are connected to each other or to the chamber and channel of claim 15. Without conceding the Examiner’s views, but rather for the purposes of expediting the prosecution of the present application, the Applicants have amended claims 17, 18 and 19, without prejudice, in efforts to address the Examiner’s concerns and to clarify the scope and meaning of the claims.

d) Claim 20 – page 4, first full paragraph

The Examiner has objected to claim 20 for not indicating how the inlet and outlet ports are connected to any other recited or unrecited components of the device. Without conceding to the Examiner’s views, but only for the purposes of expediting the prosecution of the present application, the Applicants have made clarifying amendments to claim 20 without prejudice.

e) Claim 21 – page 5, fifth paragraph

The Examiner is of the opinion that it is not clear whether “overall area” refers to “average area,” “total area,” “largest area” or some other measurement as previously recited. Applicants note that claim 21 has been canceled, without prejudice. Applicants also note, however, that claim 15 has been

amended to incorporate that feature of claim 21, such that the objection might now be extended to claim 15 as presently recited.

The Applicants respectfully disagree with the Examiner's objection. Specifically, a person of ordinary skill in the art referring to the specification and drawings (e.g., at page 25, lines 25-27 and Figures 9 and 10) would immediately understand that "overall area" refers to "average area." Nevertheless, without conceding to the Examiner's views, but rather for the purposes of expediting the prosecution of the present application, the Applicants have presently amended claim 15 to refer to the "average cross-sectional area" of the tissue disruption channel.

f) Claim 22 – page 5, sixth paragraph

The Examiner states that claim 22 is confusing because the limitations of claim 22 imply method steps whereas claim 22 is drawn to a device. Without conceding to the Examiner's views, but rather for the purposes of expediting the prosecution of the present application, the Applicants have made clarifying amendments to claim 22 in a manner such as to address the concerns of the Examiner.

g) Claim 23 – page 5, seventh paragraph

Without conceding to the Examiner's objection, but only for the purposes of expediting the prosecution of the present application, the Applicants have agreed to implement the Examiner's proposed amendment to claim 23.

In view of the above, the Applicants submit that the Examiner's concerns have been fully addressed and requests the Examiner to reconsider and withdraw the rejections under 35 U.S.C. § 112, second paragraph, and to deem the presently recited claims to be in condition for allowance.

Rejection under 35 USC § 102 over Findlay et al.

The Examiner has rejected claims 15, 17, 18, 20-22, 27, 31 and 32 as being anticipated by Findlay *et al.* (1993, *Clinical Chemistry* 39: 1927-1933) (hereinafter referred to as "Findlay") for the reasons provided at pages 6-7 of the Office Action.

In response, the Applicants respectfully disagree with the Examiner's views. Applicants observe that amended claim 15, reciting the feature of the region of constriction and the feature that the region of constriction has a smaller cross-sectional area as compared to the average cross-sectional area of the tissue disruption channel, is clearly not disclosed in Findlay. As there is no disclosure of these features in Findlay, claim 15 cannot thereby be anticipated by Findlay.

Further, the Examiner is of the opinion that the claimed apparatus does not recite any structural differences from the prior art apparatus. Applicants refer to MPEP § 2114, which states that even if the prior art device performs all the functions recited in the claim, the prior art will not anticipate the claim, if there is any structural difference. Applying this principle to claim 15, Applicants note that Findlay does not disclose the present feature of a region of constriction, wherein the tissue disruption channel at the region of constriction has a smaller cross-sectional area as compared to the average cross-sectional area of the tissue disruption channel. Thus, there is indeed a clear structural difference between the prior art apparatus and the apparatus of the present invention. As such, claim 15 is not anticipated by Findlay.

For the reasons provided above, dependent claims 17-20, 22, 23, 27, 31 and 32 are also not anticipated by Findlay, as these claims are directly or indirectly dependent on claim 15.

Rejection under 35 USC § 103 over Findlay *et al.* in view of Bjornson *et al.*

The Examiner has objected to claims 15, 17-23, 27, 31 and 32 as being unpatentable over Findlay taken in view of Bjornson *et al.* (2001, US Patent No 6,284,113) (hereinafter referred to as “Bjornson”) for the reasons provided at pages 7 to 10 of the Office Action.

Applicants respectfully disagree with the Examiner’s opinion. As discussed above, there is no disclosure in Findlay of a region of constriction, such that the tissue disruption channel has a smaller cross-sectional area within the region of constriction as compared to the average cross-sectional area of the tissue disruption channel. Findlay refers to an automated system for PCR. A person of ordinary skill in the art would understand that a PCR system would require a DNA template or a DNA gene to begin the PCR amplification process. In contrast, the device of the present invention is to obtain nucleic acid molecules (*i.e.*, the end target result of the present invention relates to the basic starting point of a PCR reaction), and accordingly, a person of ordinary skill in the art would not be motivated to look at the system disclosed in Findlay, which teaches an automated amplification system of DNA, if that person were looking to arrive at a way for obtaining the DNA. Furthermore, Bjornson only refers to a device for liquid transfer, and not a device for isolating cells and nucleic acid molecules from a tissue sample. Accordingly, a person of ordinary skill in the art would similarly *not* be motivated to refer to the teachings of Bjornson in an effort to develop a device for isolating cells and/or nucleic acid molecules from tissue samples.

The Examiner further states that a person of ordinary skill in the art would be motivated to combine the teachings of Findlay and Bjornson, and that a person of ordinary skill in the art, referring to Bjornson, would have a reasonable expectation of prospective success of placing lytic solution into the apparatus disclosed in Findlay apparatus, contending that the Findlay apparatus uses enzymes (specifically, *Taq* polymerase). Applicants respectfully disagree with this contention. As discussed above, a person of ordinary skill in the art would not be motivated to refer to the teachings of *either Findlay or Bjornson*. However, even if the person of ordinary skill in the art combined the teachings of the two documents and placed lytic solution into the apparatus disclosed in Findlay, or even modified the size and shape of the chambers and channels in the apparatus disclosed in Findlay based on alleged suggestions to do so by Bjornson, a person of ordinary skill in the art would still not be able to arrive at the device of claim 15, given the absence of teaching or suggestion in either Findlay or Bjornson to provide at least one region of constriction in the tissue disruption channel in order to disrupt a tissue sample. In fact, neither of the two documents even generally teaches or suggests what type of feature would enable the disruption of tissue samples.

To reiterate, the most critical absence from the disclosures of Findlay or Bjornson is that there is no prior teaching of providing a region of constriction within the device to disrupt tissue, as there is with the present invention. It is only with the presently disclosed device (of claim 15), that by providing at least one region of constriction, a hydrodynamic shear force is thus applied to the tissue sample going through the tissue disruption channel, thereby isolating the cells and/or nucleic acid molecules from the tissue sample without breaking the cells and releasing RNAs from the cells.

In sum, and for the reasons provided above, the cited Findlay and Bjornson references do not render obvious the present disclosure, whether considered independently or taken together. A practitioner of average skill in the art would not possess the suggestion or motivation to combine the teachings of the cited references, and even *assuming arguendo*, that such motivation were presumed, the practitioner would still lack the innovations (*e.g.*, the region of constriction within the tissue disruption channel) that are first presented with the present disclosure. In truth, it is only with the present disclosure that one of average skill in the art would recognize and understand the value of using the present device, and be able to readily put the invention into practice without further undue effort. The Examiner is thus respectfully requested to reconsider and withdraw the rejection of presently recited claims 15, 17-23, 27, 31 and 32 under 35 U.S.C. § 103 over Findlay *et al.* in view of Bjornson *et al.*

Summary

Entry of this Amendment into the file of the application is respectfully requested. The remarks presented above are believed to be sufficient to overcome all of the objections and rejections to the claims of the present application. The Examiner is, therefore, respectfully requested to reconsider and withdraw the subject rejections and to pass the application through to an allowance

If the Examiner does not agree, however, but believes that an interview would advance the progress of this case, the Examiner is respectfully invited to telephone applicants' representative at the number below so that an interview may be scheduled.

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RCF/AGG:stb

Respectfully submitted,



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